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09/529,617	06/07/2000	NIGEL J. FORROW	6237.US.01	8065

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EXAMINER
OLSEN, KAJ K

ART UNIT	PAPER NUMBER
1744	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,617	FORROW ET AL.	
	Examiner	Art Unit	
	Kaj Olsen	1744	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 6 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 6 would appear to have redundant limitations. Because claim 5 is now dependent off of claim 1, which specified the presence of binders and fillers, it would appear to be unnecessary to specify that the use of binders and fillers in claim 6 as well. Applicant needs to at least make clear whether the binders and fillers of claim 6 are the same or different materials of claim 1 (i.e. refer to them as --said-- binders and fillers).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-3 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geng et al, "Amperometric biosensors based on dehydrogenase/NAD and heterocyclic quinones", Biosensors and Bioelectronics, 11, 1996, pp. 1267-1275 (hereafter "Geng") in view of MacFarlane et al (USP 5,212,622) and Carter et al (USP 5,628,890).

7. Geng discloses an electrode-based sensor for the detection of glucose in an aqueous sample. The sensor comprises an electrode having a nicotinamide cofactor dependent enzyme glucose dehydrogenase (GDH), a cofactor of nicotinamide adenine dinucleotide (NAD/NADH), and a mediator of 1,10-phenanthroline quinone that reads on one of the claimed formulae (see introduction and section titled "Chemical and materials", pp. 1267-68). Although Geng does not explicitly identify formulating the active electrode filler and binder ingredients, MacFarlane teaches that it is conventional in the art to incorporate filler and binder materials in the electrode in order to prevent the ionic and electroactive material loss (col. 1, lines 53-61 and col. 2, line 61 through col. 4, line 11). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of MacFarlane for the sensor of Geng in order to increase sensor stability and thereby improve sensor performance. The monotonic performance of the sensor over the claimed concentration range would appear to be function of the increased stability of the sensor that was rendered obvious by the teaching of MacFarlane. In

addition, Geng indicates the sensor can be made monotonic over the claimed range (see solid squares in fig. 10 and the summary on p. 1274).

8. With respect to the limitations drawn to the use of the various supports, conductive tracks with reference and counter electrodes, all these specified elements are conventional aspects of electrode strip construction. Carter shows a protocol for constructing strip sensors and provides a sensor where the location of the sample delivery can be controlled making the sensor easy for the user to manipulate (see fig. 1 and the associated discussion therein). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Carter for the sensor of Geng and MacFarlane because the protocol of Carter is conventional in the art and provides a sensor that is easy for the user to manipulate. Geng utilizes 200 mV.

9. With respect to new claim 12, Geng also teaches the use of 1,7-phenanthroline quinone

10. Claims 1-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Batchelor in view of Geng, MacFarlane, and Carter.

11. Batchelor teaches an electrode-based sensor for the detection of 3-hydroxybutyrate (3-OHB) that utilizes 3-hydroxybutyrate dehydrogenase (HBDH), an NAD/NADH cofactor, and a quinone mediator (see fig. 1). Said quinone mediator does not read on either of the claimed formulae. The previously discussed Geng teaches that phenanthroline quinones, which do read on the claimed formulae, have low redox potentials and can oxidize NADH efficiently (see section titled "cyclic voltammetry of heterocyclic quinones", p. 1269). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the

teaching of Geng for the sensor of Batchelor because the identified mediator of Geng can readily oxidize NADH at low redox potentials thereby improving sensor performance.

12. With respect to the limitations drawn to the use of fillers, binders, and various strip components, MacFarlane teaches that it is conventional in the art to incorporate filler and binder materials in the electrode in order to prevent the ionic and electroactive material loss (col. 1, lines 53-61 and col. 2, line 61 through col. 4, line 11). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of MacFarlane for the sensor of Batchelor and Geng in order to increase sensor stability and thereby improve sensor performance. The monotonic performance of the sensor over the claimed concentration range would appear to be function of the increased stability of the sensor that was rendered obvious by the teaching of MacFarlane. In addition, Batchelor shows a monotonic and substantially linear response from 1-8 mM of analyte (fig. 3).

13. With respect to the limitations drawn to the use of the various supports, conductive tracks with reference and counter electrodes, all these specified elements are conventional aspects of electrode strip construction. Carter shows a protocol for constructing strip sensors and provides a sensor where the location of the sample delivery can be controlled making the sensor easy for the user to manipulate (see fig. 1 and the associated discussion therein). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Carter for the sensor of Batchelor, Geng, and MacFarlane because the protocol of Carter is conventional in the art and provides a sensor that is easy for the user to manipulate.

14. With respect to the claims drawn to the process of using the electrode, Batchelor demonstrates very clearly in fig. 1 how the various components of the sensor interact with each

other. In particular, fig. 1 shows how the dehydrogenase oxidizes the analyte in the presence of NAD. The NAD is reduced to NADH and subsequently reoxidized by the quinone mediator. A potential applied to the electrode causes the mediator to reoxidize where the resultant current is monotonically related to the concentration of analyte (i.e. two electrodes for every analyte molecule (see also fig. 3)).

15. With respect to the use of GDH, Geng already disclosed the use of GDH for amperometric biosensors (see discussion above) and Geng teaches the use of 200 mV for phenanthroline quinones.

16. Claims 4-11, and 14 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Geng in view of MacFarlane and Carter as applied to claims 1 and 2 above, in further view of (or as evidence by) Batchelor.

17. With respect to claim 4, the references set forth the limitations of the claim, but did not explicitly identify the use of HBDH as the cofactor-dependent enzyme. Geng recognizes the utility of the described glucose sensor for other sensing applications utilizing NAD(P) cofactors (see title and introduction). Batchelor teaches an analogous sensor which utilizes the enzyme 3-hydroxybutyrate dehydrogenase which is thereby capable of measuring 3-hydroxybutyrate (see abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Batchelor for the sensor of Geng in order to extend the utility of the sensor of Geng to additional compounds such as 3-hydroxybutyrate.

18. With respect to the claims drawn to the method of using the electrode of claim 1 (those limitations not already discussed above), Geng set forth the various components of the sensor and teaches how the various components interact to provide the sensor. However, Geng doesn't

set forth the various claimed steps of oxidation and reduction for the sensor as clearly as Batchelor did (see discussion above). The diagram shown by Batchelor is the same protocol utilized for Geng with the substitution of 3-OHB and HBDH in the diagram for glucose and GDH respectively. In this instance, Batchelor is being utilized solely to evidence what Geng already teaches (just not as pictorially as Batchelor does). With respect to claim 10, Geng recognizes the utility of the described glucose sensor for other sensing applications utilizing NAD(P) cofactors (see title and introduction). Batchelor teaches an analogous sensor which utilizes the enzyme 3-hydroxybutyrate dehydrogenase which is thereby capable of measuring 3-hydroxybutyrate (see abstract). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Batchelor for the sensor of Geng in order to extend the utility of the sensor of Geng to additional compounds such as 3-hydroxybutyrate.

19. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geng, McFarlane, and Carter (with or without evidence by Batchelor) as applied to claims 1 and 5 above, and further in view of Itoh et al (Chemistry Letters, vol. 8, 1992, pp. 1583-1586).

20. Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Batchelor, Geng, McFarlane, and Carter as applied to claims 1 and 5 above, and further in view of Itoh.

21. With respect to the claims, Geng does appear to suggest that the device with the specific mediators taught (i.e. the 1,10 and 1,7 forms) could be extended to any general form of the phenanthroline quinone beyond the two specific forms discussed (see "Cyclic voltammetry of heterocyclic quinines", p. 1269). However, Geng did not explicitly teach the use of 4,7-

phenanthroline quinone. Itoh teaches in an alternate sensor that the 4,7-, 1,7-, and 1,10- forms of phenanthroline quinone all find utility in NAD recycling systems (fig. 1). In particular, the 4,7 form showed the highest catalytic efficiency of any of the forms of phenanthroline quinone (see paragraph below fig. 1 on p. 1584). It would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the teaching of Itoh for the sensor of Geng, McFarlane, and Carter (or Batchelor, Geng, McFarlane, and Carter) in order to garner an increased catalytic efficiency.

Response to Arguments

22. Applicant's arguments filed on 4-26-2002 have been fully considered but they are not persuasive. Applicant urges that the problem addressed by MacFarlane is not the same problem as addressed by the instant invention. In particular, MacFarlane is related to ion transfer and not mediators as taught by Geng. However, MacFarlane is more generally related to the prevention of electroactive compounds placed within an electrode from leaching out when the electrode is exposed to an aqueous sample (col. 1, lines 48-61). This is precisely relevant for the teachings of Geng and Batchelor that are drawn to biosensors for aqueous materials such as blood or urine (e.g. see Batchelor, p. 289) that have electroactive materials that are not covalently bound to the electrode surface and would thereby be susceptible to leaching. Applicant also urges that even if it would have been obvious to combine the teaching of MacFarlane with either Geng or Batchelor, one still would not have known that the combination would have provided the unexpected results. However, it has been well established that a patent cannot be granted for the discovery of a result, even though it may be unexpectedly good, which would flow logically

from the teaching of the prior art. In this case, MacFarlane teaches that the addition of binders and fillers prevent electroactive materials from leaching out of the electrode (see discussion above). Furthermore, if by "unexpected", the applicant is referring to the limitations drawn to the sensor being monotonic over the particular analyte range, the examiner points out that this limitation does not read free of the responses of the sensors of Geng and Batchelor even without the binder and filler elements (see Geng, fig. 10 and Batchelor, fig. 3).

23. With respect to the teaching of Batchelor, applicant also discusses at length why one of ordinary skill in the art would not utilize the material 4-methyl-o-quinone (4-MQ) including the fact that the material is highly light sensitive and is very reactive. Although this may all be true, the examiner fails to understand the relevance of these points. The molecule 4-MQ does not read on the defined mediator of claim 1 (4-MQ does not have R1 and R2 groups that are aromatic or heteroaromatic groups as set forth by claim 1). What the examiner's rejection using Batchelor concerned was that it would have been obvious to one of ordinary skill in the art at the time the invention was being made to utilize the mediator of Geng (i.e. a mediator that reads on the claimed invention) for the sensor of Batchelor because the identified mediator of Geng can readily oxidize NADH at low redox potentials thereby improving sensor performance (see discussion above and in the previous office action). Applicant's discussion of why one would avoid the use of 4-MQ would appear to only further render obvious why one would look to the mediators set forth by Geng.

24. Applicant also urges that one would not have looked to the use of 1,10-phenanthroline and 1,7-phenanthroline quinones over the material Meldola's Blue prior to the applicant's invention. This is confusing because Geng specifically anticipates the use of these materials (see

rejection above). Anticipation is the epitome of obviousness (see *In re Skoner* 186 USPQ 80; *In re Peterson* 181 USPQ 641; *In re Kalm* 154 USPQ 10, 12). Applicant urges that one of ordinary skill would not have known from the teachings of Geng that these quinones do not inhibit NAD-dependent hydrogenase enzymes and thereby provide a longer shelf life. However, Geng specifically taught the use of these mediators for the specific hydrogenase enzymes in question. Whether Geng (or one possessing ordinary skill in the art) recognized these particularly favorable properties for these particular enzymes is irrelevant in view of the fact that the prior art recognized these combinations of materials. Discovering a new reason for combining two materials that were already anticipated by the prior art as being combined does not impart patentability over said prior art.

Conclusion

25. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kaj Olsen whose telephone number is (703) 305-0506. The examiner can normally be reached on M-F 8:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Warden Sr. can be reached on 703-308-2920. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3599 for regular communications and (703) 305-5408 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Kaj K. Olsen
Patent Examiner
AU 1744
July 24, 2002

Robert J. Warden, Sr.

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